BlueCross BlueShield Association

An Association of
Independent Blue Cross
and Blue Shield Plans

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March 22, 2000

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Comments on Proposed Criteria for Classifying OTC Drugs
Docket No. 96N-0277

Dear Sir or Madam:

On behalf of the Blue Cross Blue Shield Association (BCBSA), which represents 49 independent Blue Cross and Blue Shield Plans that provide health coverage for 75 million Americans, I thank you for the opportunity to submit comments in response to the Food and Drug Administration's ("FDA") proposed rule on additional criteria for classifying over-the-counter drugs as generally recognized as safe and effective and not misbranded ("Proposed Rule").[1]

BCBSA supports the basic tenets of the proposed rule, particularly FDA's proposal to allow foreign marketing information and data ("foreign data") to be used to establish that certain "conditions" (active ingredient, dosage form, etc.) used in OTC drug products marketed abroad are eligible for inclusion in OTC drug monographs. The rule, as proposed, would allow such foreign marketing data to be considered only if the condition is a component of an OTC drug marketed abroad – and *may not* be considered if such a condition is limited to prescription drug use in the United States. Proposed 21 C.F.R. 330.14(b)(2) ("a condition is not eligible for OTC drug monograph status if marketing in the United States is limited to prescription drug use"). BCBSA urges the FDA to modify the proposed rule to allow for consideration of foreign marketing experience for conditions limited to prescription drug use in the United States.

FDA Should Expand Proposed Criteria for Inclusion in OTC Drug Monographs to Drugs Marketed as Prescription Drugs in the U.S. Under the proposed rule, FDA excludes conditions marketed as prescription drugs in the U.S. from consideration of inclusion in an OTC drug monograph, based on the assumption that these conditions are per se unable to meet statutory requirements.[2] A drug is eligible for OTC status, if the drug is: (1) generally recognized as safe and effective (GRAS/E); and (2) used to a material extent and for a material time.[3] FDA may determine drugs to be eligible for an OTC drug monograph as GRAS/E on the basis of various types of evidence, including "significant human experience during marketing."[4]

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[1] 64 Fed. Reg. 71062 (Dec. 20 1999).

[2] Id. at 71080 ("a condition is not eligible for OTC drug monograph status if marketing in the United States is limited to prescription drug use").

[3] See 21 U.S.C. § 321(p).

[4] 21 C.F.R. § 330.10(a)(4).

Therefore, if provided with adequate evidence, FDA has the authority to determine if any condition is eligible for an OTC drug monograph. In light of this broad framework, FDA should not automatically assume that conditions marketed in the U.S. as prescription are unable to be determined GRAS/E or used to a material extent or for a material time. Indeed, during the original OTC drug review process of drugs marketed prior to 1972, certain prescription conditions were added to the OTC monographs.

In the Proposed Rule, FDA recognizes that foreign data may provide the evidence required to determine if a drug marketed outside the U.S. is eligible for inclusion in an OTC drug monograph. It is unclear why such data may not establish why a condition marketed as prescription in the U.S. cannot meet OTC drug monograph requirements. Indeed the Supreme Court has determined that a GRAS/E determination is one of science, rather than geography and therefore a finding of general safety may rest in whole or part on foreign data.[5] Such a conclusion is also supported by the FFDCA's "new drug" definition, which draws no distinction between U.S. and foreign data.[6] These same foreign data may establish that the drug is GRAS/E, in conformance with the definition of safety and effectiveness of conditions in OTC drugs.[7] In our view, the public is better served by FDA permitting consideration of foreign data in determining whether a condition marketed for U.S. prescription drug use may be eligible for inclusion in an OTC drug monograph.

It is important to note FDA's position in the Advanced Notice of Proposed Rulemaking ("ANPR") published on October 3, 1996, that an NDA is the best mechanism for a prescription to OTC "switch," as the manufacturer may exert control when the drug is first marketed as an OTC and because there are adverse event reporting controls in place.[8] In the ANPR, FDA also acknowledges that, "if and when an adverse event reporting system for OTC monograph drugs is established, this system would better support the use of OTC drug monographs for future prescription to OTC switches that do not require critical manufacturing controls for safe and effective use."[9] Indeed, the Proposed Rule requires adverse event reporting for foreign data, even though there are currently no such requirements for OTC drugs marketed in the United States.[10] However, if adequate adverse event information are available for foreign OTC drugs that remain marketed as prescription drugs in the U.S., FDA should allow the consideration of these active substances and products for the possible inclusion in an OTC drug monograph.

Expanding the OTC Monograph Process Would Allow the Public Greater Access to Safe "Switched" Drugs. A drug that is appropriate for OTC use may remain a prescription drug unless the manufacturer identifies incentives to make a "switch." The majority of "switches" are accomplished by the manufacturer via a new drug application (NDA) or a Supplement. The second method for a "switch," the original OTC drug review and monograph program established in 1972, remains inapplicable to drugs that are marketed as prescriptions drugs after

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[5] See Fmali Herb, Inc. v. Heckler, 715 F.2d 1385 (9th Cir. 1983).

[6] 21 U.S.C. § 321.

[7] See, e.g., 21 C.F.R. § 330.10(a)(4) ("Safety means a low incidence of adverse reactions or significant side effects . . . Proof of safety shall consist of adequate tests by [reasonable] methods . . .This proof shall include results of human experience during marketing . . .").

[8] See 61 Fed. Reg. 51625, 51629 (Oct. 3, 1996).

[9] Id.

[10] See 64 Fed. Reg. 71062, 71081.

1972. Finally, the third method, the individually initiated petition for a change in status, also remains unlikely to succeed unless initiated by the manufacturer, as the manufacturer controls most of the safety and use information to support such a switch.

In conclusion, we urge FDA to modify the proposed rule to allow foreign marketing data to be considered for conditions that are included in foreign OTC drugs, but marketed as prescription in the United States. Such a modification would allow the public access to conditions that would be appropriate for switch. Since manufacturers significantly control the decision to pursue OTC marketing, many prescription conditions that could conceivably meet the requirements for marketing OTC, nevertheless remain marketed as a prescription drugs. The drug monograph system, however, presents a veritable method whereby third parties, as well as manufacturers, may request a "switch" for drugs from prescription to OTC status, especially when adequate foreign data are available. Such a system ultimately will result in providing the public with access to drugs that are appropriately marketed OTC.

Please call Julie Miller of my staff (202.626.8625) if you have any questions regarding this letter. We look forward to a continuing dialogue with the FDA on this issue.

Sincerely,

Mary Nell Lehnhard
Senior Vice President

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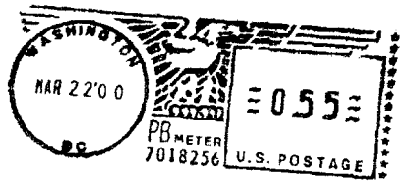

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